

CLAIMS:

1. A method of tolerising a cell population to a target antigen, comprising contacting said cell population with

(a) a tolerogenic peptide sequence from EBV LMP1 or LMP2 protein, or a nucleic acid encoding said tolerogenic peptide sequence such that said tolerogenic peptide sequence is expressed in said cell population; and

(b) the target antigen, or a nucleic acid encoding said target antigen such that said target antigen is expressed in said cell population;

wherein said cell population comprises mononuclear leukocytes from a subject seropositive for EBV.

2. A method according to claim 1, comprising the steps of contacting a population of antigen presenting cells with said tolerogenic peptide sequence and said target antigen, and subsequently contacting said cell population with said population of antigen presenting cells.

3. A method according to claim 1 or claim 2, wherein said mononuclear leukocytes are contacted with said tolerogenic peptide sequence and said target antigen *in vitro*.

4. A method according to claim 3, wherein said cell population or a subset thereof is re-administered to said subject after contacting with said tolerogenic peptide sequence and said target antigen.

5. A method according to claim 2, wherein said population of antigen presenting cells is contacted with said tolerogenic peptide sequence and said target antigen *in vitro* and said cell population is contacted with said population of antigen presenting cells *in vivo*.

6. A method according to claim 1, wherein said tolerogenic peptide sequence and said target antigen are administered directly to said subject.

5 7. A method according to any one of claims 1 to 6, wherein the tolerogenic peptide sequence comprises one or more of the sequences P2, P4, P7, P14, P15, P18, P20, P22, P23, P24 and P32.

10 8. Use of EBV LMP1, LMP2, a tolerogenic peptide sequence thereof, or a nucleic acid encoding the same, in the preparation of a medicament for the tolerisation of an individual against a target antigen, wherein the medicament further comprises the target antigen or a nucleic acid encoding the target antigen, and wherein the individual has previously been infected with EBV.

15 9. Use according to claim 8, wherein the medicament comprises the target antigen or a nucleic acid encoding the target antigen.

20 10. Use according to claim 8 or claim 9 wherein the target antigen is a cell.

11. Use according to claim 10 wherein the cell is for transplantation.

25 12. Use according to claim 11 in combination with claim 9 wherein the cell comprises nucleic acid encoding the tolerogenic peptide sequence.

30 13. Use according to any one of claims 8 to 12 wherein the tolerogenic peptide sequence comprises one or more of the sequences P2, P4, P7, P14, P15, P18, P20, P22, P23, P24 and P32.

35 14. A pharmaceutical composition, for tolerising a subject against a target antigen, comprising EBV LMP1, LMP2, a tolerogenic peptide sequence thereof, and the target antigen or nucleic acid encoding the target antigen, in admixture with a pharmaceutically

acceptable carrier, wherein the subject has previously been infected with EBV.

15. A method for assessing the tolerogenicity of a test peptide sequence from an infectious agent, comprising the steps of:

(i) contacting a cell population with said test peptide sequence,

(ii) determining whether IL-10 expression in said cell population is increased, and optionally

(iii) correlating the result of step (ii) with the tolerogenicity of the sequence,

wherein said cell population comprises mononuclear leukocytes from a donor previously infected by said infectious agent.

16. A method according to claim 15, wherein said cell population comprises at least one type of antigen presenting cell.

17. A method according to claim 15 or claim 16, wherein said mononuclear leukocytes comprise at least T lymphocytes, B lymphocytes, natural killer (NK) cells, monocytes, macrophages or dendritic cells.

18. A method according to claim 17, wherein said mononuclear leukocytes comprise at least CD4<sup>+</sup> T lymphocytes.

19. A method according to claim 18, wherein said mononuclear leukocytes further comprise at least one type of antigen presenting cell.

20. A method according to any one of claims 15 to 19, further comprising the steps of:

(i) (a) contacting a similar cell population from a donor not previously infected by said infectious agent with said test peptide sequence; and

5 (ii) (a) determining whether IL-10 expression in said cell population is increased,

and optionally

10 (ii) (b) comparing the results from step (ii) with the results from step (ii) (a).

21. A method according to any one of claims 15 to 20, wherein the infectious agent is a virus.

15

22. A method according to claim 21, wherein the virus is a herpesvirus encoding a viral IL-10 homologue

23. A method according to claim 22, wherein the virus is EBV.

20

24. A method according to claim 23, wherein the test peptide sequence is derived from EBV LMP1 protein or LMP2 protein.

25. A method according to claim 24, wherein the test or tolerogenic peptide sequence comprises one or more of the sequences P1 to P75 or P1' to P96'.

25

26. A method for assessing the tolerogenicity of a test peptide sequence from an infectious agent towards a target antigen, comprising the steps of:

30

(i) contacting a cell population with (a) said test peptide sequence and (b) a target antigen, to make a test composition,

35 (ii) re-contacting the cell population from said test composition with said target antigen in the absence of said test peptide sequence,

(iii) assessing cell proliferation or expression of IL-4, IL-2, IL-12 or gamma-IFN by said cell population in response to said target antigen, and optionally

(iv) correlating the result of step (iii) with the tolerogenicity of the test peptide sequence.

wherein said cell population comprises mononuclear leukocytes from a donor previously infected by said infectious agent.

27. A method according to claim 26, further comprising the step of adding fresh antigen presenting cells prior to step (ii).

28. A method according to claim 26 or claim 27, further comprising the step of contacting the cell population with a confirmatory antigen unrelated to the test sequence or the target antigen.

29. A method according to any one of claims 26 to 28, wherein the infectious agent is a virus.

30. A method according to claim 29, wherein the virus is a herpesvirus encoding a viral IL-10 homologue

31. A method according to claim 30, wherein the virus is EBV.

32. A method according to claim 31, wherein the test peptide sequence is derived from EBV LMP1 protein or LMP2 protein.

33. A method according to claim 32, wherein the test or tolerogenic peptide sequence comprises one or more of the sequences P1 to P75 or P1' to P96'.

34. A method for assessing the tolerogenicity of a test peptide sequence, comprising the steps of:

(i) contacting a first cell population with said test peptide sequence,

(ii) contacting a second cell population with a control peptide sequence

(iii) determining whether IL-10 expression in each said cell population is increased, and optionally

(iv) correlating the result of step (iii) with the tolerogenicity of the test peptide sequence,

wherein each said cell population comprises mononuclear leukocytes from a donor previously infected by an infectious agent, and said control peptide sequence is derived from said infectious agent.

35. A method according to claim 34 wherein said control peptide sequence has previously been identified to induce IL-10 expression in a cell population comprising mononuclear leukocytes from a donor previously infected by said infectious agent.

36. A method according to claim 34 or claim 35, wherein said first and second cell populations are derived from the same donor.

37. A method according to claim 36, wherein said first and second cell populations comprise a T cell clone capable of proliferating in response to the control peptide.

38. A method according to any one of claims 34 to 37, wherein said infectious agent is EBV.

39. A method according to claim 39, wherein said control peptide is derived from LMP1 or LMP2.

40. A peptide having the sequence of any one of P2, P4, P5, P6, P7, P8, P9, P10, P12, P13, P14, P15, P16, P17, P18, P20, P22, P23, P24, P25, P26, P27, P29, P30, P32, P34, P35, P39, P68, P71, P72.